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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,759	07/10/2001	Avi Ashkenazi	10466/59	9581

9157 7590 05/20/2003

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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	19

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/902,759	Askhenazi et al
Examiner	**Art Unit**
Mosher	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *8/26/2002, 2/19/2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39-44* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39-44* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *13*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alignment*

DETAILED ACTION

Priority

Applicants have provided the requested information regarding parent applications. The preliminary amendment filed August 26, 2002, amending page 1 of the specification also clarified the priority claim; this amendment was matched with the file after the 9/23/2002 Office action was mailed.

Claim Rejections - 35 USC § 112

On reconsideration, the rejection of claims 39-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is WITHDRAWN.

Applicants argue that the present application and the earliest priority application disclose that the PRO246 polypeptide shares significant homology to the human Coxsackie-adenovirus receptor, and that a portion of the PRO246 polypeptide has a significant homology with the human cell surface protein HCAR (note, HCAR is an acronym for the human Coxsackie-adenovirus receptor). Considering its significant homology, applicants suggest PRO246 to be a novel cell surface viral receptor. Applicants argue that HCAR was well-known, and virus assays were well known in the art, as evidenced by Tomko et al and by Example X of US 5,942,606. These arguments are is not convincing, for the following reasons. Alignment of applicant's sequence with the human and mouse HCAR proteins indicates an overall similarity of 17%, and a

best local similarity of 27%, see the attached sequence alignments. McNicholl et al is cited as evidence that a protein with 100% homology to a portion of a virus receptor does not function as a virus receptor (e.g. the truncated CCR5), and Struyf et al is cited as evidence that alteration of even a few amino acids degrades the ability of another receptor to interact with a virus. Carson is cited as evidence that the N-terminal region of CAR physically complexes with adenovirus; alignment of applicant's sequence with CAR shows little or no homology in the N-terminal region, suggesting that applicant's protein does not possess a critical feature necessary for activity as an adenovirus receptor. Cohen et al is cited as evidence that the C-terminal region of CAR is not required for adenovirus receptor activity; see page 25395; alignment of applicant's sequence indicates that this nonessential C-terminal region of CAR is the region most homologous to applicant's protein. With the large degree of divergence between applicant's protein and the most similar known virus receptor, there is ample reason for one skilled in the art to doubt an unsupported assertion of virus receptor activity. The specification provides no evidence that the claimed protein actually can function as a viral receptor, and fails to teach any virus which interacts with the putative receptor. The examiner maintains that, absent knowledge of which virus(es) interact with a receptor, one skilled in the art is not able to use the receptor for any routine virological purpose. As to the argument that assays such as those of Tomko et al could be routinely used to identify the specific viruses that use this polypeptide as a receptor, Tomko et al were in possession of an antibody known to interfere with Coxsackie/adenovirus infection, and identified the receptor by its ability to bind the antibody. Tomko provides no assay able to

determine which virus, if any, will interact with a novel protein. It is also notable that Tomko did a functional assay "To determine whether the HCAR and MCAR cDNAs truly encoded functional receptors" (page 3354), indicating scepticism in this art in the absence of a showing of functional activity.

Applicant further cites Example X of US 5,942,606 as evidence of knowledge of routine virus assays at the earliest priority date. A US patent cannot be used as evidence of routine knowledge in the art prior to its publication date, because a patent necessarily discloses something which is not routine. Applicant further argues that the disclosure of US 5,942,606 is very similar to the disclosure of the present application, and the issuance of the presumptively valid patent is prima facie evidence that such experimental data are not required to comply with the requirements of patentability. To this argument, the examiner can only reply that each application is examined on its own merits, and in this application, this applicant has not convincingly rebutted the prima facie conclusion of nonenablement of the disclosed protein as a virus receptor.

HOWEVER, the instant specification does disclose that PRO246 protein has a biological activity of inhibiting VEGF-stimulated epithelial cell growth, see Assay 9 at specification pages 204-205. Although the specification does not refer to this particular biological activity in its discussion of the antibody claimed in this application, on reconsideration it is concluded that one skilled in the art would, without undue experimentation, be able to use a protein with this demonstrated biological activity, and consequently would be able to use an antibody which binds to the protein. Therefore, the enablement rejection is WITHDRAWN.

Claim Rejections - 35 USC § 102

Claims 39-44 are rejected under 35 U.S.C. 102(e2) as being anticipated by Lal et al 5,942,606, for reasons of record. Applicant's argument that they are entitled to an early priority date is not convincing; the disclosure in the earliest priority document does not enable any use for the claimed products, for the same reasons as the instant disclosure fails to enable use of PRO246 as a virus receptor.

However, the rejection under 35 U.S.C. 102(b) is withdrawn, for the following reasons. The disclosure of anti-VEGF biological activity, which enables use of the PRO246 protein and antibody, is present in parent application PCT/US98/18824 filed 9/10/1998, which is prior to the publication date of the Lal patent.

The following reference is cited as of interest, in disclosing a polypeptide similar to SEQ ID NO:39. No copy is provided, because the patent is exceedingly bulky.

US20030027998 INTERCEPT 258, SEQ 76.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 15, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600